

### REMARKS

Claims 1-8, 10, 21-22, 24 and 26 have been amended to incorporate the features of claim 9 and Claim 11 has been amended to depend from claim 1. Also, claim 1 is amended to delete the "wherein" clause regarding the method of the coating. See new claim 27. No new matter has been added.

#### **Claim Rejections under 35 U.S.C. §102**

Applicants' claims 1-3 and 5-6 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by U.S. Patent 4,780,450, to Sauk et al.; and claims 1-3 and 5-8 have been rejected under 35 U.S.C. §102(b) as allegedly being anticipated by U.S. Patent 5,573,771, to Geistlich et al. Also, claims 5,7-8 and 24-26 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent 5,205,921 to Shirkanzadeh. These rejections are rendered moot by amending the claims to be implant claims rather than coating for implant claims.

Claims 1-3, 5, 7-10 and 22-23 have been rejected under 35 U.S.C. §102(b) as allegedly being anticipated by U.S. Patent 5,543,441, to Rhee et al, claims 1-3, 5, 9-10 and 21-23 have been rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Worch et al (US 6,524,718) and claims 1-3, 5, 9-10 and 21-23 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by U.S. Patent 5,205,921 to Shirkanzadeh. Applicants respectfully traverse these rejections.

Rhee teaches implants coated with a collagen-polymer conjugate. The collagen, preferably reconstituted atelopeptide collagen, is chemically bonded to a synthetic hydrophilic polymer, preferably polyethylene glycol, to form a collagen-polymer conjugate. For bone repair, the conjugate may be applied in combination with calcium phosphate. Following the teachings of Rhee one skilled in the art would not arrive at a coated implant of the present invention. The coatings of Rhee are functionalized collagen-polymer-conjugates and not collagen matrix mineralized with a calcium phosphate. Thus, the statement at the bottom of page 6 of the Office

Action that Rhee et al. "teach a composition containing the recited components *of* a collagen matrix mineralized with calcium phosphate" is incorrect.

Worch describes an electrochemical coating process, which forms a two-layered system. The outer layer comprises an organic and/or inorganic phase. The organic phase may contain collagen and the inorganic phase may be calcium phosphate. The organic and/or inorganic component becomes incorporated into the metallic oxide phase such that the polyphase oxide coating compares with an alloy (see column 2, lines 55-59 and Examples 1 and 2). The coatings of Worch are embedded in the oxide surface of the implant. They do not form a mineralized collagen outer layer coating deposited on the implant surface. Nor does Worch et al. describe a process for producing a mineralized collagen matrix.

Shirkanzadeh describes an electrochemical process for depositing bioactive coatings, such as calcium phosphate or aluminum oxide, onto conductive substrates. An electrolyte bath containing an aqueous solution of the desired oxide or phosphate is prepared with an inert anode. A titanium implant may be used as the cathode. The electrolyte may further contain collagen. At Examples 1-5 of Shirkanzadeh it is noted that the calcium phosphate coating layer is characterized by either micro pores or is without pores. At col.3, lines 46-48 of '921 it is pointed out that the micro pores of the calcium phosphate layer encourage adhesion of macro molecules, such as collagen. Such a structure is shown in Figure 1, as published by Shirkanzadeh in 1992 in Material Letters, volume 14, pages 27-30, a copy of which is attached. The crystals exhibit a crystal size of approximately 5-10  $\mu\text{m}$ , which are too large to promote mineralization. Thus, the collagen component of Shirkanzadeh is not mineralized with a calcium phosphate phase and does not resemble native bone material. Thus a calcium phosphate layer according to Shirkanzadeh does not resemble native bone material as determined by the FTIR-spectra shown in attached Figure 2.

In the Office Action, at page 5, the Examiner alleges that applicants have not provided evidence to prove a structural difference and that there is no structurally distinguishing feature

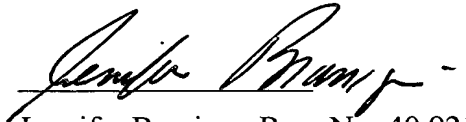
compared to the prior art. The structurally distinguishing physical characteristics of applicants bone analogous coating, as examined by electron microscopic, are discussed in examples 1-4 of the specification. Applicants collagen matrix, which is mineralized with calcium phosphate by precipitating calcium phosphate from a solution in the presence of collagen, has definite physical properties (e.g., permeable structure) which are analogous to the structure of bone produced in vivo, and further exhibits good adhesion directly onto metallic implant surfaces.

The coated implant of applicants invention is based on a biometric process wherein the mineralized collagen is formed under conditions found in vivo. In this process, hydroxyapatite is formed by calcium and phosphate ions from an electrolyte solution transforming from an amorphous phase to a crystalline hydroxyapatite and yielding a collagen-calcium phosphate interconnected layer with a three dimensional structure. The structure, as determined by REM, can be seen in attached Figure 3. It can be seen that the calcium phosphate molecules and molecule aggregates are located not only on the site of the collagen layer but also between and on the collagen fibrils enabling the 3D structure that resembles native bone. As compared to Figure 1, the crystals in Figure 3 have a size of less than 1  $\mu\text{m}$ . The FTIR spectrum shown in Figure 4, attached, shows the similarity of natural bone and mineralized collagen. As can be seen, mineralized collagen is not just the simple mixture of calcium phosphate and collagen, but rather a distinct structurally unique phase.

Thus, Worch, Shirkanzadeh and Rhee do not teach a coated metallic implant having a collagen matrix mineralized with a calcium phosphate phase. Therefore, it is respectfully requested that the rejections under 102 should be withdrawn.

In view of the amendments and above remarks, favorable consideration is courteously requested. However, if there is any remaining issue(s) which can be expeditiously resolved by a telephone conference, the Examiner is courteously requested to telephone the undersigned at the number indicated below.

Respectfully submitted,



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